

AMENDMENT

Please amend this application as follows:

IN THE CLAIMS

1. (Thrice Amended) An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence as set forth in SEQ ID NO: 1;
- (b) a nucleotide sequence encoding the polypeptide set forth in SEQ ID NO: 2; and
- (c) a nucleotide sequence ^{fully} complementary to either of (a) or (b).

2. (Thrice Amended) An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence encoding a polypeptide that is at least 95 ⁹⁵ percent identical to the polypeptide set forth in SEQ ID NO: 2, wherein the encoded polypeptide has at least 1,649 amino acids and has human E3 α ubiquitin ligase activity of the polypeptide set forth in SEQ ID NO: 2; and

(b) ~~a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide sequence as set forth in SEQ ID NO: 1, encoding a polypeptide that has human E3 α ligase activity of the polypeptide set forth in SEQ ID NO: 2;~~

(c) ^{fully} a nucleotide sequence complementary to any of (a)-(b).

3. (Thrice Amended) An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence encoding a polypeptide set forth in SEQ ID NO: 2 with at least a substitution of one to 100 conservative amino acid acids substitution, wherein the polypeptide has human E3 α ubiquitin ligase activity of the polypeptide set forth in SEQ ID NO: 2;

E (b) ~~a nucleotide sequence encoding a polypeptide set forth in SEQ ID NO:~~
E ~~2 with at least an insertion of one to 100 amino acid acids insertion, wherein the~~
E ~~polypeptide has human E3 α ubiquitin ligase activity of the polypeptide set forth in~~
E ~~SEQ ID NO: 2, and optionally comprises a truncation and/or deletion up to about 100~~
E ~~amino acids;~~

E ^b
E ^a
E (c) a nucleotide sequence encoding a polypeptide set forth in SEQ ID NO:
E 2 with at least ~~an internal~~ ^a deletion of one to 100 amino acid acids ^{deletion}, wherein
E the polypeptide has ~~human~~ E3 α ubiquitin ligase activity of the polypeptide set forth in
E SEQ ID NO: 2;

E ^c
E (d) a nucleotide sequence encoding a polypeptide set forth in SEQ ID NO:
E 2 which has a C- and/or N-terminal truncation ^{up to about 100 amino acids}, wherein
E the polypeptide has ~~human~~ E3 α ubiquitin ligase activity of the polypeptide set forth in
E SEQ ID NO: 2;

E ^d
E (e) a nucleotide sequence encoding a polypeptide set forth in SEQ ID NO:
E 2 with at least a ^{modification} of one to 100 amino acids ~~modification~~ selected from
E the group consisting of amino acid substitutions, amino acid insertions, amino acid
E deletions, C-terminal truncation, and N-terminal truncation, wherein the polypeptide
E has ~~human~~ E3 α ubiquitin ligase activity of the polypeptide set forth in SEQ ID NO: 2;
E and

E ^e
E (f) ^{fully} a nucleotide sequence complementary to any one of (a)-(e).

D2 4. (Amended) A vector comprising the nucleic acid molecule of any one
of claims 1, 2, or 3.

5. (Original) A host cell comprising the vector of claim 4.

6. (Original) The host cell of claim 5 that is a eukaryotic cell.

7. (Original) The host cell of claim 5 that is a prokaryotic cell.

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8. (Amended) A process of producing a ~~huE3 α human~~ E3 α ubiquitin ligase polypeptide comprising culturing the host cell of claim 5 under suitable conditions to express the polypeptide, ~~and optionally isolating the polypeptide from the culture.~~

D3

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E

E

9 10. (Amended) The process of claim 8, wherein the nucleic acid molecule comprises promoter ~~DNA other than the promoter DNA for the native huE3 α human~~

E3 α ubiquitin ligase polypeptide operatively linked to the DNA encoding the huE3 α

~~human E3 α ubiquitin ligase~~ polypeptide.

wherein said promoter is not native human E3 α ubiquitin ligase promoter

11. (Original) The isolated nucleic acid molecule according to claim 2 wherein the percent identity is determined using a computer program selected from the group consisting of GAP, BLASTP, BLASTN, FASTA, BLASTA, BLASTX, BestFit, and the Smith-Waterman algorithm.

10

46.

(Amended) A composition comprising a nucleic acid molecule of any one of claims 1, 2, or 3 and a ~~pharmaceutically acceptable formulation agent.~~

47. (Original) A composition of claim 46 wherein said nucleic acid molecule is contained in a viral vector.

12

48.

(Amended) A viral vector comprising a nucleic acid molecule of any one of claims 1, 2, or 3.

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59. (Thrice Amended) A reagent comprising a detectably labeled
E nucleic acid molecule
D7 E polynucleotide encoding the amino acid sequence set out in SEQ ID NO: 2; or allelic
1 variants or splice variants thereof with human E3 α ligase activity according to any
E one of claims 1 to 3.
1, 2 or 3

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61. (Twice Amended) A method for determining the presence of huE3 α a
human E3 α ubiquitin ligase nucleic acids acid in a biological sample comprising the
steps of:

(a) providing a biological sample suspected of containing huE3 α a human
E3 α ubiquitin ligase nucleic acids acid;

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59 (b) contacting the biological sample with a the reagent according to claim
D8 59 under conditions wherein the reagent will hybridize with huE3 α a human E3 α
ubiquitin ligase nucleic acids acid contained in said biological sample;

(c) detecting hybridization between huE3 α the human E3 α ubiquitin
ligase nucleic acid in the biological sample and the reagent; and

(d) comparing the level of hybridization between the nucleic acid in the
biological sample and the reagent with the level of hybridization between a known
concentration of huE3 α human E3 α ubiquitin ligase nucleic acid and the reagent.

16
62. (Twice Amended) A method for detecting the presence of huE3 α a
human E3 α ubiquitin ligase nucleic acids acid in a tissue or cellular sample
comprising the steps of:

D9 (a) providing a tissue or cellular sample suspected of containing huE3 α a
human E3 α ubiquitin ligase nucleic acids acid;

13 (b) contacting the tissue or cellular sample with a the reagent according to
claim 59 under conditions wherein the reagent will hybridize with huE3 α a human
E3 α ubiquitin ligase nucleic acids acid;

(c) detecting hybridization between ~~huE3~~ the human E3 α ubiquitin ligase nucleic acid in the tissue or cellular sample and the reagent; and

(d) comparing the level of hybridization between the nucleic acid in the tissue or cellular sample and reagent with the level of hybridization between a known concentration of ~~huE3~~ human E3 α ubiquitin ligase nucleic acid and the reagent.

63. (Original) The method of claim 59 wherein said polynucleotide molecule is DNA.

64. (Original) The method of claim 59 wherein said polynucleotide molecule is RNA.

19 67
^ 65. (New) An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

(a) the nucleotide sequence as set forth in SEQ ID NO: 18;

(b) a nucleotide sequence encoding the polypeptide set forth in SEQ ID NO: 19; and

(c) a nucleotide sequence ^{fully}complementary to either of (a) or (b).